REMARKS

In the last Office Action, the Examiner objected to the drawings because the measurement for cubic centimeters is not designated in the metric system as required by PCT Rule 10.1(a). Claims 1-3 were rejected under 35 U.S.C. §103(a) as being unpatentable over European Patent No. 0926482 A3 to Matsui et al. ("Matsui") in view of U.S. Patent No. 5,242,837 to Slovacek et al. and U.S. Patent No. 4,055,768 to Bromburg. Additional art was cited of interest.

In accordance with the present response, the specification has been suitably revised to correct informalities, provide antecedent basis for the claim language, and bring it into better conformance with U.S. practice. The specification has been further revised to provide a cross-reference for copending International Application Ser. No. PCT/JP00/06342. Original claims 1-3 have been replaced with new claims 4-6 to correct informalities, bring them into better conformance with U.S. practice, and further patentably distinguish from the prior art of record. New claims 7-16 have been added to provide a fuller scope of coverage. The title of the invention has been changed to "APPARATUS FOR IMAGING FLUORESCENT PARTICLES" to more clearly reflect the invention to which the new claims are directed. A new, more descriptive abstract has been substituted for the original abstract.

Submitted herewith are replacement sheets for Figs. 1 and 2 incorporating revisions to conform Fig. 1 to the revised specification and to overcome the drawing objection with respect to Fig. 2. More specifically, Fig. 1 has been revised to designate with reference numerals the interior space 3b, exterior surface 3c, side wall 3d, bottom wall 3e, entry surface A, and entry surface B of the imaging container 3. In Fig. 2, "cc" has been changed to "cm^3."

Applicants respectfully request reconsideration of their application in light of the following discussion.

Brief Summary of Invention

The present invention is directed to an apparatus for imaging fluorescent particles.

In the field of medical treatment, blood platelet derivatives and red blood cell derivatives have been manufactured by extracting blood platelets and red blood cells from blood. These blood platelet derivatives and red blood cell derivatives are each used for blood transfusions, and it is not desirable to have white blood cells mixed therein. For this reason, it is important to know the number of white blood cells that are mixed in with such derivatives. Conventionally, a sample of blood platelet derivative dyed with a fluorescent dye is placed on a slide glass plate referred to as a Nageotte chamber and irradiated with

illuminating light and the number of white blood cells is counted using a microscope. Specifically, the number of white blood cells in a 50 microliter sample is counted and converted to the number of white blood cells in the whole bag. This is a time-consuming task that has to be performed by an experienced person, and such work is extremely inefficient and tiring.

Moreover, in a conventional apparatus for imaging fluorescent particles (e.g., white blood cells), the fluorescent particles are dyed with a fluorescent dye and are collected at the bottom of an imaging container. Only a portion near the bottom of the imaging container is irradiated with exciting light, thereby exciting the fluorescent particles. Thereafter, the bottom part of the imaging container is imaged from the bottom and the fluorescent particles are counted.

The foregoing conventional apparatus for imaging fluorescent particles is useful when used for items such as blood platelet derivatives, blood plasma derivatives, and spinal fluid that have a high transmittance to exciting light. Furthermore, in the case of red blood cell derivatives, centrifugal force is used to separate red blood cells and white blood cells, and the removal rate is low, at around 10%, leaving a large quantity of white blood cells mixed in. In this case, the red blood cell derivative is diluted and the

reduced number of white blood cells in a micro-sample is counted. However, there is no need for dilution in the case of red blood cell derivatives in which there is a low count of entrained white blood cells. This exhibits a low transmittance to exciting light, and the white blood cells collecting at the bottom are not uniformly irradiated by the exciting light, making it difficult to count them correctly.

The present invention overcomes the drawbacks of the conventional art by providing an apparatus for imaging fluorescent particles that can correctly count the number of fluorescent particles even when the measurement target substance has a different transmittance to exciting light.

Figs. 1-2 show an embodiment of an apparatus for imaging fluorescent particles according to the present invention embodied in the claims. The apparatus has an imaging container 3 having an interior space 3b, an exterior surface 3c, an upper portion 3a, and a bottom portion 3' having a side wall 3d and a bottom wall 3e for collecting fluorescent particles. A part of the exterior surface 3c of the imaging container 3 corresponding to the side wall 3d of the bottom portion 3' defines a first entry surface B of the imaging container 3 for receiving an excitation beam of light. A part of the exterior surface 3c of the imaging container 3 corresponding to the bottom wall 3e of the bottom portion 3' defines a second entry surface A of the imaging container 3

for receiving an excitation beam of light. A light generating device 1 generates an excitation beam of light for exciting the fluorescent particles collected in the bottom portion 3' of the imaging container 3. A first illumination device (e.g., diffuser 2) irradiates the excitation beam of light generated by the light generating device 1 onto the first entry surface B of the imaging container to illuminate the fluorescent particles collected in the bottom portion 3' of the imaging container 3. A second illumination device (e.g., mirror 21 and diffuser 22) irradiates the excitation beam of light generated by the light generating device 1 onto the second entry surface A of the imaging container 3 to illuminate the fluorescent particles collected in the bottom portion 3' of the imaging container 3.

A switching device includes an optical element 20 which is movable between a first position in which the optical element is removed from an optical path of the excitation beam of light and a second position in which the optical element is disposed in the optical path of the excitation beam of light. In the first position, the optical element 20 causes the excitation beam of light to be irradiated onto the first entry surface B of the imaging container 3. In the second position, the optical element is disposed in the optical path of the excitation beam of light so that the excitation beam of light is irradiated onto the second entry surface A of the imaging

container. An imaging device 12-14 captures images of the illuminated fluorescent particles from the bottom wall 3e of the imaging container 3.

By the foregoing construction, the apparatus for imaging fluorescent particles according to the present invention can correctly count the number of fluorescent particles collected on the bottom portion 3′ of the imaging container 3 even when the measurement target substance has a different transmittance to exciting light. For example, if the fluorescent particles on the bottom portion 3′ of the imaging container have a high transmittance to exciting light, the optical element 20 is removed from the optical path of the excitation beam of light (i.e., the optical element 20 is placed in the first position), causing the excitation beam of light to be irradiated onto the first entry surface B of the imaging container 3. In this case, the fluorescence of the particles is prevented from acting as disturbing light.

In contrast, if the fluorescent particles have a low transmittance to exciting light, the optical element 20 is placed in the optical path of the excitation beam of light (i.e., the optical element 20 is placed in the second position), causing the excitation beam of light to be irradiated onto the second entry surface A of the imaging container 3. In this case, since the transmittance of the fluorescent particles is low, the exciting light reaches only

the bottom and the portion near the bottom of the imaging container 3, and fluorescence acting as background light is hardly produced.

Applicants respectfully submit that the prior art of record does not disclose or suggest the subject matter recited in newly added claims 4-16.

Newly added independent claim 4 is directed to an apparatus for imaging fluorescent particles stained with a fluorescent dye and requires an imaging container having an interior space, an exterior surface, an upper portion, and a bottom portion having a side wall and a bottom wall for collecting fluorescent particles, a part of the exterior surface of the imaging container corresponding to the side wall of the bottom portion defining a first entry surface of the imaging container for receiving an excitation beam of light, and a part of the exterior surface of the imaging container corresponding to the bottom wall of the bottom portion defining a second entry surface of the imaging container for receiving an excitation beam of light. Claim 4 further requires light generating means for generating an excitation beam of light for exciting the fluorescent particles collected in the bottom portion of the imaging container, first illumination means for irradiating the excitation beam of light generated by the light generating means onto the first entry surface of the imaging container to

illuminate the fluorescent particles collected in the bottom portion of the imaging container, second illumination means for irradiating the excitation beam of light generated by the light generating means onto the second entry surface of the imaging container to illuminate the fluorescent particles collected in the bottom portion of the imaging container, switching means for switching between the first illumination means to irradiate the excitation beam of light generated by the light generating means onto the first entry surface of the imaging container and the second illumination means to irradiate the excitation beam of light generated by the light generating means onto the second entry surface of the imaging container, and an imaging device for capturing images of the illuminated fluorescent particles from the bottom wall of the imaging container.

The prior art of record does not disclose or suggest the structural combination of the apparatus recited in independent claim 4. For example, Matsui discloses an apparatus for imaging fluorescent particles in which only a side surface (i.e., entry surface) of a bottom portion 3' of an imaging container 3 is irradiated with an excitation beam of light to illuminate fluorescent particles collected in the bottom portion of the imaging container 3 (Fig. 1). Stated otherwise, Matsui discloses means (e.g., laser light source 1 and diffuser plate 2) for irradiating only the side surface

(i.e., only one entry surface) of the bottom portion 3' of the imaging container 3. In contrast, independent claim 4 requires first illumination means for irradiating the excitation beam of light generated by the light generating means onto the first entry surface of the imaging container to illuminate the fluorescent particles collected in the bottom portion of the imaging container and second illumination means for irradiating the excitation beam of light generated by the light generating means onto the second entry surface of the imaging container to illuminate the fluorescent particles collected in the bottom portion of the imaging container.

Thus, while Matsui discloses means for for irradiating an excitation beam of light onto only one entry surface of the imaging container 3, claim 4 requires means (first and second illumination means) for selectively irradiating the excitation beam of light onto two entry surfaces of the imaging container. Again, Matsui discloses means for irradiating a side surface at a bottom portion of the imaging container 3, but does not disclose means for irradiating both a side surface and a bottom wall at the bottom portion of the imaging container, as required by independent claim 4.

Moreover, claim 4 further requires switching means for switching between the first illumination means to irradiate the excitation beam of light generated by the light

generating means onto the first entry surface of the imaging container and the second illumination means to irradiate the excitation beam of light generated by the light generating means onto the second entry surface of the imaging container. As recognized by the Examiner, this structure and corresponding function is clearly not disclose or suggested by Matsui.

Each of the cited references to Slovacek and Bromberg discloses a light measuring device and teaches the irradiation of a bottom wall or front face of an imaging container. In the rejection of original independent claim 1, now the subject matter of independent claim 4, the Examiner contends that it would have been obvious to one of ordinary skill in the art to modify the apparatus of Matsui in view of Slovacek and Bromberg by adding a second irradiation means for irradiating a bottom wall of the imaging container 3 in order to improve the analysis flexibility of the apparatus. Applicants vigorously disagree with the Examiner's contention.

As recognized by the Examiner, Slovacek and Bromberg disclose means for irradiating only a bottom wall or front face (i.e., one entry surface) of an imaging container. Stated otherwise, Slovacek and Bromberg do not disclose or suggest means for irradiating a side wall at the bottom portion of the imaging container. Thus, as set forth above with respect to Matsui, there is simply no teaching in

Slovacek and Bromberg of means for irradiating both a side surface and a bottom wall at a bottom portion of the imaging container, as required by independent claim 4.

Moreover, even if it were proper to modify Matsui in view of Slovacek and Bromberg as proposed by the Examiner, the proposed combination would result in an apparatus for irradiating only a bottom wall at the bottom portion of the imaging container, which is not the invention recited in independent claim 4.

Thus independent claim 4 is not rendered obvious by Matsui, Slovacek and Bromberg because the references do not suggest the modifications that would be needed to replicate the claimed invention. In the context of obviousness rejections based upon the purported obviousness of effecting a required modification, the Federal Circuit has held that "[t]he mere fact that the prior art may be modified in [a given] manner ... does not make the modification obvious unless the prior art suggested the desirability of the modification". In re Fritch, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992). There is nothing in the references to Matsui, Slovacek and Bromberg that would have suggested modifying the structure of the Matsui's apparatus to achieve the structure of the apparatus discussed above and recited by independent claim 4.

New independent claims 9 and 12 are also directed to an apparatus for imaging fluorescent particles and require

light projecting means for selectively projecting an excitation beam of light onto the first entry surface of the imaging container to illuminate the fluorescent particles or onto the second entry surface of the imaging container to illuminate the fluorescent particles. No corresponding structure and function is disclosed or suggested by the prior art of record as set forth above for independent claim 4.

Claims 5-8, 10-11 and 13-16 depend on and contain all of the limitations of independent claims 4, 9 and 12, respectively, and, therefore, distinguish from the references at least in the same manner as claims 4, 9 and 12.

In view of the foregoing amendments and discussion, the application is believed to be in allowable form. Accordingly, favorable reconsideration and allowance of the claims are most respectfully requested.

Respectfully submitted,

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